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Early esophageal neuroendocrine tumor

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ABSTRACT

Esophageal neuroendocrine tumors are rare and often found incidentally on endoscopy. We present a unique case of an esophageal neuroendocrine tumor found in the setting of dysplasia associated with Barrett's esophagus. The tumor was removed endoscopically. This case highlights the incidence, prognosis, and management of esophageal neuroendocrine tumors.

KEYWORDS Endoscopic mucosal resection; esophagus; neuroendocrine tumor

Esophageal neuroendocrine tumors are rare, comprising 1.6% of all newly diagnosed neuroendocrine tumors.[1] These tumors are typically sporadic but can be associated with multiple neuroendocrine neoplasia-1 and other rare genetic disorders.[2] While the gastrointestinal tract is the most frequent primary site, these tumors can be seen throughout the body.[3] A recent study found that on endoscopic evaluation, 77% of esophageal neuroendocrine tumors were found in the lower third of the esophagus, with a mean size of 2.3 cm at the time of diagnosis.[4] Most patients are asymptomatic, but approximately 25% present with dysphagia. Very few patients present with the typical Cushing's syndrome that is widely taught in medical training. The size of the tumor and extent of involvement are of paramount importance when determining treatment strategies for patients with esophageal neuroendocrine tumors. Here, we report a case of an early neuroendocrine tumor found in the esophagus treated with complete endoscopic resection.

CASE REPORT

A 71-year-old white woman with Barrett's esophagus diagnosed in 2002 was referred for management of high-grade dysplasia identified on esophageal biopsies on a prior endoscopy. The patient reported a long-standing history of gastroesophageal reflux disease, but her symptoms were controlled with proton pump inhibitor therapy. She denied any symptoms of dysphagia, nausea, vomiting, abdominal pain, melena, hematochezia, diarrhea, or weight loss. At endoscopy, a 1 mm area of suspected neoplasia with disruption of the mucosal pattern was identified using narrow-band imaging with near focus imaging *(Figure 1)*. Endoscopic mucosal resection (EMR) was performed in the area without complications.

The histology from the EMR specimen demonstrated a 1 mm tumor with cells in both nest and rosette pattern extending into the muscularis mucosa *(Figure 2)*. The cells were positive for chromogranin, synaptophysin, and cytokeratin on immunohistochemical staining. Additionally, Ki-67 was <2%. These histologic findings were consistent with a well-differentiated neuroendocrine tumor. There were negative margins on the resected specimen, and a computed tomography scan showed no evidence of metastatic disease. Oncology concluded that the tumor was a primary distal esophageal neuroendocrine tumor that was completely resected by EMR with negative margins. The rest of the biopsy specimens obtained with a mapping protocol were consistent with Barrett's esophagus, with focal low-grade dysplasia but no evidence of high-grade dysplasia or esophageal adenocarcinoma. The patient completed endotherapy and is in her second year of surveillance without evidence of recurrence of either dysplasia or tumor.

DISCUSSION

Esophageal neuroendocrine tumors are rare, with variable prognosis based on the extent of disease at the time of diagnosis. A recent study in Korea found patients diagnosed with esophageal neuroendocrine tumors to have a median survival of 27 months, with a tumor size of >2 cm being a negative

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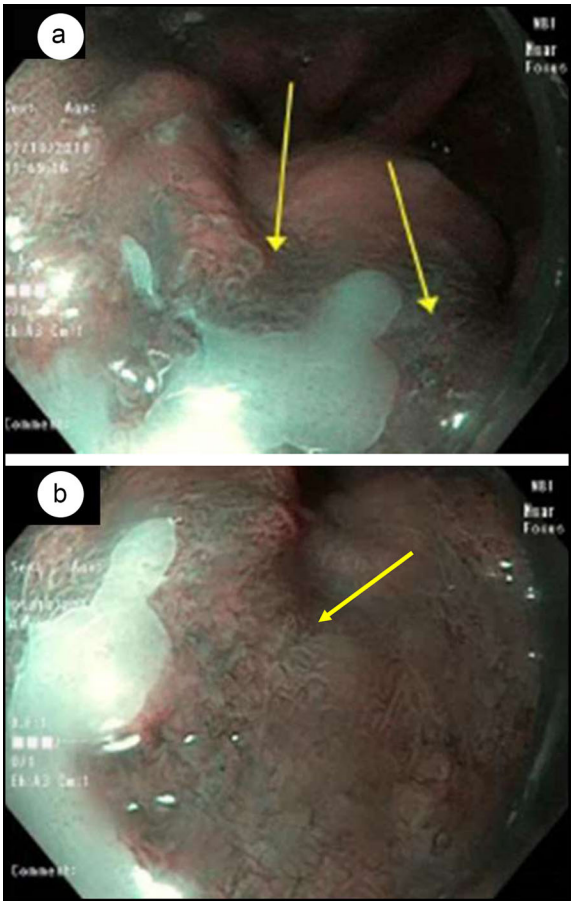

Figure 1. **(a)** Endoscopic view with narrow band imaging of mucosal irregularity (arrows), which was found to be an esophageal neuroendocrine tumor. **(b)** Mucosal irregularity on narrowing band imaging with irregular cellular pattern and disruption of typical villous pattern (arrow).

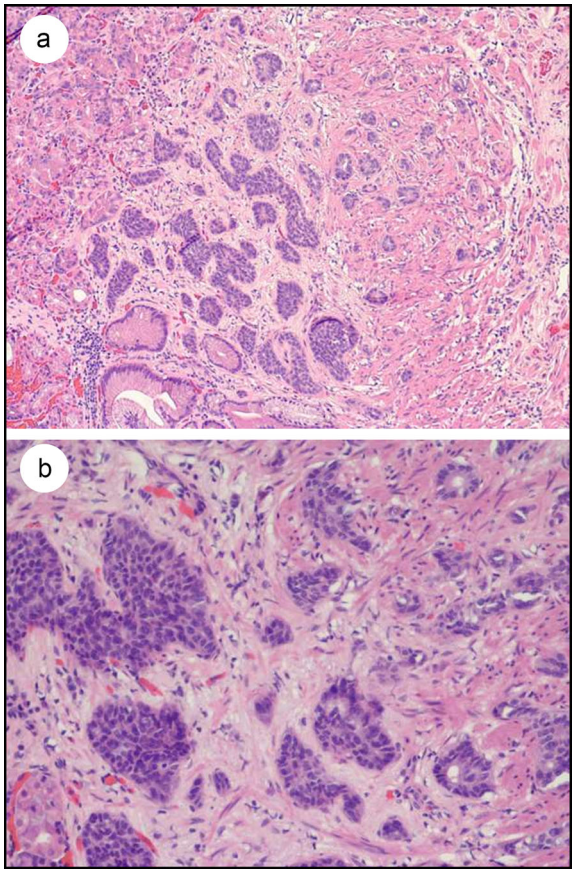

Figure 2. **(a)** Photomicrographs (hematoxylin and eosin stain) showing **(a)** tumor cells invading into the muscularis mucosa (20×) and **(b)** nests and rosette pattern of tumor cells (40×).

prognostic factor for poor survival and metastasis. Overall, 1-year survival of patients with well-differentiated esophageal neuroendocrine tumors (noncarcinomas) is 100%, compared to 85% for well-differentiated neuroendocrine carcinomas and 33% for poorly differentiated neuroendocrine carcinomas.[4]

These tumors are primarily diagnosed by esophagogastroduodenoscopy with biopsy. Staging of disease is obtained through use of imaging (computed tomography, magnetic resonance imaging, and positron emission tomography) and histologic classification based on biopsy results. Appropriate staging is necessary to select an appropriate therapeutic regimen.

The mainstay of therapy is surgical resection with or without adjuvant therapy. If surgery is not an option, then chronic medical management to alleviate symptoms and to suppress tumor growth and spread is recommended. Palliative debulking surgery is also a possibility. Liver lesions can be treated with ablative therapies such as transarterial embolization, transarterial chemoembolization, and selective internal radiation therapy with Y-90 microspheres. Systemic therapy with somatostatin analogs, peptide receptor radionuclide therapy, low-dose interferon, everolimus, sunitinib, bevacizumab, and cytotoxic regimens is also available.[4,5]

To date, there have been only a few case reports of neuroendocrine tumors in the setting of Barrett's esophagus, with most also having esophageal adenocarcinoma. In patients with Barrett's esophagus, EMR has been used to treat dysplasia and avoid progression to adenocarcinoma. One of the advantages of EMR is the ability to obtain a large intact histologic specimen, which in this case led to the diagnosis and treatment of a well-differentiated esophageal neuroendocrine tumor. This case is unique in that an esophageal neuroendocrine tumor was found at an early stage due to the targeting of irregularities found in the esophagus with EMR based on the history of Barrett's-associated dysplasia.

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